REMARKS

Claims 1-9, 11-14, and 17-24 are pending in the application. Applicants have cancelled claims 10-16, 18-21, and 23-24 without prejudice. Claims 1-9, 17, and 22 will therefore be pending upon entry of the proposed amendments.

Applicants have deleted the phrase "solvate or *in vivo* hydrolysable ester" from claims 1-9, 17, and 22. Applicants have also deleted the first occurrence of "optionally" in the definition of R^1 in claims 1, 2, and 6. As such, the present claims require that R^1 must be a **substituted** C_{3-7}carbocyclyl, a **substituted** C_{1-8}alkyl, a **substituted** C_{2-6}alkenyl, or a **substituted** C_{2-6}alkynyl group. Support for this amendment can be found throughout the specification, e.g., at page 7, lines 15-22 and the title compounds of Examples 1-34.

No new matter is introduced by these amendments.

The foregoing amendments are being made for the sole purpose of expediting prosecution of the present application. Applicants expressly reserve the right to pursue any cancelled subject matter in a later filed continuing application.

Rejections under 35 U.S.C. § 112, first paragraph

I. Claims 1-9, 11-14, and 17-24 are rejected for allegedly failing to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. According to the Office (Office Action, page 2):

> [T]he specification, while being enabling for a compound of formula (I) or a pharmaceutically acceptable salt thereof, does not reasonably provide enablement for a solvate or in vivo hydrolysable ester of a compound of formula (I). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants respectfully disagree with the grounds for the rejection; however, to expedite prosecution, Applicants have deleted the phrase "solvate or *in vivo* hydrolysable ester" from

claims 1-9, 17, and 22 and cancelled claims 11-14, 18-21, and 23-24. In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

II. Claims 11-12, 14, 19-21, and 23-24 are rejected for allegedly failing to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. According to the Office (Office Action, page 9):

> [T]he specification, while being enabling for the treatment of rheumatoid arthritis and osteoarthritis, does not reasonably provide enablement for a method of treating allergic rhinitis, asthma, COPD, inflammatory bowel disease, etc.; or a method of treating cancer; or a method of treating a disease or condition in which modulation of chemokine receptor activity is beneficial; or a method of combination therapy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants respectfully disagree with the grounds for the rejection; however, to expedite prosecution, Applicants have cancelled claims 11-12, 14, 19-21, and 23-24, thus rendering the rejection moot.

Rejections under 35 U.S.C. § 112, second paragraph

I. Claims 1-9, 11-14, and 17-24 are rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection states, in part (Office Action, page 17-18):

> [T]he definition of various substituents groups on pyrimidine include such groups, namely esters, etc., see e.g., the definition of R^2 wherein the carbocyclyl is substituted with $-COOR^7$ wherein R^7 is hydrogen, alkyl or phenyl. Therefore, the instantly claimed formula (1) already includes esters, which are *in vivo* hydrolysable and also, the corresponding acids. Therefore it is not clear what is the difference between these variable groups and the "m vivo hydrolysable ester" groups. The use of ester group(s), etc. as substituents as well as in *'in vivo hydrolysable ester'* as Markush choice, results in ambiguity.

Applicants respectfully disagree with the grounds for the rejection; however, to expedite prosecution, Applicants have deleted the phrase "*in vivo* hydrolysable ester" from claims 1-9, 17,

and 22 and cancelled claims 11-14, 18-21, and 23-24. In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

II. Claims 1-9, 11-14, and 17-24 are rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to the Office (Office Action, page 18, emphasis in original):

> Claim 18 recites the limitation "converting the compound of formula (1) into a further compound of formula (1), ... iv) **forming a prodrug**" in all the steps (a) to (d), see e.g., lines 7-10 of the claim. There is insufficient antecedent basis for this limitation in claim 1 on which claim 18 is dependent. Claim 1 does not recite 'a prodrug' of the compound of formula (1).

Applicants respectfully disagree with the grounds for the rejection; however, to expedite prosecution, Applicants have cancelled claim 18, thus rendering the rejection moot.

III. Claim 19 is rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to the Office (Office Action, page 18):

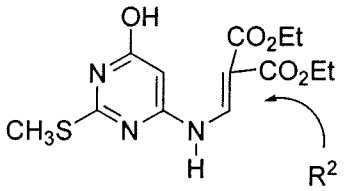
> Claim 19 is drawn to 'a method of combination therapy', however, the claim does not set forth the precise metes and bounds of the claim. The claim does not properly recite the type of 'patient or subject' to which the combination therapy is provided. It is not clear what is intended by the term "other therapy" in the claim.

Applicants respectfully disagree with the grounds for the rejection; however, to expedite prosecution, Applicants have cancelled claim 19, thus rendering the rejection moot.

Rejections under 35 U.S.C. § 102

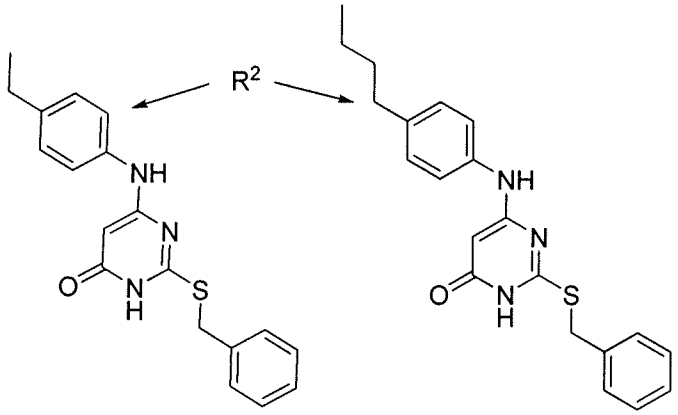
I. Claims 1-2, 4-5, 8, and 17 are rejected under U.S.C. 102(b) as being anticipated by Minami et al., U.S. Patent No. 3,673,184 (the '184 patent). The Office relies on the disclosure of "the compound 4 in Table II" (Office Action, page 18) in the '184 patent as the

basis for the rejection. For the convenience of the Office, the chemical structure of "the compound 4 in Table II" is provided below (referred to herein as "compound 4").



As can be seen, the substituent corresponding to Applicants' R^2 in compound 4 is diethyl 2-methylenemalonate, i.e., a C_2 alkenyl group that is substituted with 2 CO_2Et groups. In contrast, the present claims require that when R^2 is C_{2-6} alkenyl, the R^2 alkenyl group must be substituted by 1, 2 or 3 substituents independently selected from hydroxy, amino, C_{1-6}alkoxy, C_{1-6}alkylamino, di(C_{1-6}alkyl)amino, *N*-(C_{1-6} alkyl)-*N*–(phenyl)amino, *N*- C_{1-6}alkylcarbamoyl, *N,N*-(C_{1-6} alkyl)$_2$carbamoyl, *N*-(C_{1-6} alkyl)-*N*–(phenyl)carbamoyl, carboxy, phenoxycarbonyl, $-NR^8COR^9$, $-SO_2R^{10}$, $-SO_2NR^5R^6$ and $-NR^8SO_2R$. As such, compound 4 does **not** fall within the scope of the present claims because Applicants' R^2 alkenyl groups **cannot** be substituted with CO_2Et. Therefore, the '184 patent does not anticipate the present claims because the '184 patent does not disclose a compound meeting all of the limitations of the present claims. In view of the foregoing, Applicants respectfully request that the rejection be reconsidered and withdrawn.

II. Claims 1-2, 4-6, 8, and 17 are rejected under 35 U.S.C. § 102(b) as being anticipated by Nogimori et al. The Office relies on the disclosure of "compounds 8 and 9 in page 1694" (Office Action, page 19) of Nogimori et al as the basis for the rejection. For the convenience of the Office, the chemical structures of "compounds 8 and 9 in page 1694" are provided below (referred to herein as "compounds 8 and 9").



The chemical structures shown above for compounds 8 and 9 were generated from the systematic names disclosed in Nogimori et al. for compounds 8 and 9, i.e., "(2-(benzylthio)-6-(*p*-ethylanilino)-4-pyrimidone" and "2-(benzylthio)-6-(*p*-*n*-butylanilino)-4-pyrimidone)" (see page 1694, column 1 of Nogimori et al.) using the ChemDraw Ultra 11.0 "convert name to structure" tool.

As can be seen, the substituents corresponding to Applicants' R^2 in compounds 8 and 9 are both alkyl-substituted phenyl groups, namely 4-ethylphenyl and 4-butylphenyl, respectively. In contrast, the present claims require that R^2 must be:

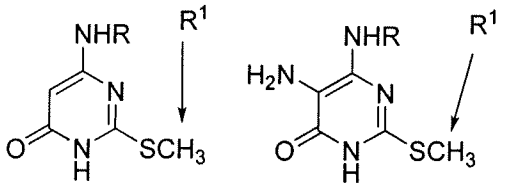
> C_{3-7}carbocyclyl, optionally substituted by 1, 2 or 3 substituents independently selected from:
>
> (a) fluoro, -OR^4, -NR^5R^6 -$CONR^5R^6$, -$COOR^7$, -NR^8COR^9, -SR^{10}, -SO_2R^{10}, -$SO_2NR^5R^6$, -$NR^8SO_2R^9$;
>
> (b) a 3-8 membered ring optionally containing 1, 2 or 3 atoms selected from O, S, -NR^8 and whereby the ring is optionally substituted by C_{1-3}alkyl or fluoro; or
>
> (c) phenyl or heteroaryl, each of which is optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, nitro, -OR^4, -NR^5R^6, -$CONR^5R^6$, -NR^8COR^9, -$SO_2NR^5R^6$, -$NR^8SO_2R^9$, C_{1-6}alkyl and trifluoromethyl; or
>
> a group selected from C_{1-8}alkyl, C_{2-6}alkenyl or C_{2-6}alkynyl wherein the group is substituted by 1, 2 or 3 substituents independently selected from hydroxy, amino, C_{1-6}alkoxy, C_{1-6}alkylamino, di(C_{1-6}alkyl)amino, *N*-(C_{1-6} alkyl)-*N* –

(phenyl)amino, *N*- C_{1-6}alkylcarbamoyl, *N,N*-(C_{1-6} alkyl)$_2$carbamoyl, *N*-(C_{1-6} alkyl)-*N* –(phenyl)carbamoyl, carboxy, phenoxycarbonyl, $-NR^8COR^9$, $-SO_2R^{10}$, $-SO_2NR^5R^6$ and $-NR^8SO_2R^9$;

Nogimori et al. does not disclose any compound meeting all of the limitations of the present claims and therefore does not anticipate the present claims. In view of the foregoing, Applicants respectfully request that the rejection be reconsidered and withdrawn.

III. Claims 1-2, 4-5, 8, and 17 are rejected under 35 U.S.C. § 102(b) as being anticipated by "JP 61-118372 (cited in the IDS) or the corresponding CAPLUS Abstract 106:18604 (1987)" (Office Action, page 19). The aforementioned references disclose compounds in which the substituent corresponding to Applicants' R^1 is an unsubstituted alkyl group (e.g., CH_3). In contrast, the claims as presently amended require that when R^1 is C_{1-8}alkyl, the R^1 alkyl group must be a substituted alkyl group. As such, the aforementioned references do not disclose a compound meeting all of the limitations of the claims as presently amended and therefore do not anticipate the claims as presently amended. In view of the foregoing, Applicants respectfully request that the rejection be reconsidered and withdrawn.

IV. Claims 1-8 and 17 are rejected under 35 U.S.C. § 102(b) as being anticipated by Huebsch et al.. The Office relies on the disclosure of "compounds 5, 6, 25, and 26 in page 1380" (Office Action, page 19) of Huebsch et al. For the convenience of the Office, the chemical structure of "compounds 5, 6, 25, and 26 in page 1380" are provided below (referred to herein as "compounds 5, 6, 25, and 26").

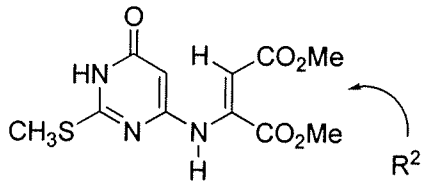


5 R= CH_3
6 R= CH_2CH_2OH
25 R= CH_3
26 R= CH_2CH_2OH

The substituent corresponding to Applicants' R^1 in compounds 5, 6, 25, and 26 is an unsubstituted alkyl group, namely CH_3. In contrast, the claims as presently amended require that when R^1 is $C_{1\text{-}8}$alkyl, the R^1 alkyl group must be a substituted alkyl group. As such, the aforementioned references do not disclose a compound meeting all of the limitations of the claims as presently amended and therefore do not anticipate the claims as presently amended. In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

V. Claims 1-8 and 17 are rejected under 35 U.S.C. § 102(b) as being anticipated by "JP 31-197467 (cited in the IDS) or the corresponding CAPLUS Abstract 115:280054 (1991)" (Office Action, page 19). The aforementioned references disclose compounds in which the substituent corresponding to Applicants' R^1 is an unsubstituted alkyl group (e.g., CH_3). In contrast, the claims as presently amended require that when R^1 is $C_{1\text{-}8}$alkyl, the R^1 alkyl group must be a substituted alkyl group. As such, the aforementioned references do not disclose a compound meeting all of the limitations of the claims as presently amended and therefore do not anticipate the claims as presently amended. In view of the foregoing, Applicants respectfully request that the rejection be reconsidered and withdrawn.

VI. Claims 1-2, 4-6, 8, and 17 are rejected under 35 U.S.C. § 102(b) as being anticipated by Cobo et al.. The Office relies on the disclosure of "the compound 10d in page 10348" (Office Action, page 19) of Cobo et al. For the convenience of the Office, the chemical structure of "the compound 10d in page 10348" is provided below (referred to herein as "compound 10d").



As can be seen, the substituent corresponding to Applicants' R^2 in compound 10d is a C_2 alkenyl group that is substituted with 2 CO_2Me groups. In contrast, the present claims require that when R^2 is C_{2-6} alkenyl, the R^2 alkenyl group must be substituted by 1, 2 or 3 substituents independently selected from hydroxy, amino, C_{1-6}alkoxy, C_{1-6}alkylamino, di(C_{1-6}alkyl)amino, *N*-(C_{1-6} alkyl)-*N* –(phenyl)amino, *N*- C_{1-6}alkylcarbamoyl, *N,N*-(C_{1-6} alkyl)$_2$carbamoyl, *N*-(C_{1-6} alkyl)-*N* –(phenyl)carbamoyl, carboxy, phenoxycarbonyl, $-NR^8COR^9$, $-SO_2R^{10}$, $-SO_2NR^5R^6$ and $-NR^8SO_2R$. As such, compound 10d does **not** fall within the scope of the present claims because Applicants' R^2 alkenyl groups **cannot** be substituted with CO_2Me. Therefore, Cobo et al does not anticipate the present claims because Cobo et al does not disclose a compound meeting all of the limitations of the present claims. In view of the foregoing, Applicants respectfully request that the rejection be reconsidered and withdrawn.

VII. Claims 1-8 and 17 are rejected under 35 U.S.C. § 102(b) as being anticipated by WO 00/76980 (cited in the IDS). The Office relies on the disclosure of "the compounds 8-1 to 8-20 in Table 3 pages 32-33" (Office Action, page 19) of WO 00/76980. The substituent corresponding to Applicants' R^1 in "compounds 8-1 to 8-20 in Table 3 pages 32-33"is an unsubstituted alkyl group, namely CH_3. In contrast, the claims as presently amended require that when R^1 is C_{1-8}alkyl, the R^1 alkyl group must be a substituted alkyl group. As such, the aforementioned references do not disclose a compound meeting all of the limitations of the claims as presently amended and therefore do not anticipate the claims as presently amended. In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

Applicants submit that all claims are in condition for allowance.

The fee in the amount of $1,050 for the three month extension fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of a Deposit Account authorization. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 06275-443US1.

Respectfully submitted,

Date: April 4, 2008

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